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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/988,113	11/19/2001	Iris Pecker	01/22781	8049

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EXAMINER

HUTSON, RICHARD G

ART UNIT PAPER NUMBER

1652,

DATE MAILED: 01/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/988,113

Applicant(s)

PECKER ET AL.

Examiner

Richard G Hutson

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 18 August 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-31 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3,8,10,11,13,18-20,22 and 27-31 is/are rejected.
- 7) ☒ Claim(s) 2,4-7,9,12,14-17,21 and 23-26 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9/2003.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

Applicants amendment of the specification, and claims 1, 6, 7, 9, 10, 11, 16, 17, 20, 25, 26, 28 and 29 and the addition of new claim 31 in the Paper of 8/18/2003, is acknowledged. Claims 1-31 are at issue and are present for examination.

Applicants' arguments filed on 8/18/2003 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

### ***Information Disclosure Statement***

Applicants filing of the information disclosure statement filed on 9/22/2003 is acknowledged. Those references considered have been initialed.

### ***Claim Objections***

Claims 2, 4-7, 9, 12, 14-17, 21 and 23-26 are objected to because of the following informalities:

Claims 2, 4-7, 9, 12, 14-17, 21 and 23-26 depend from rejected claims 1, 3, 8, 10, 11, 13, 18, 19, 20, 22, respectively.

Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 8, 10, 11, 13, 18, 19, 20, 22, 27, 28, 29, 30 and 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide fragment comprising a polynucleotide sequence encoding a polypeptide having heparanase catalytic activity, wherein said polypeptide comprises the amino acid sequence of SEQ ID NO: 10, does not reasonably provide enablement for any polynucleotide fragment comprising a polynucleotide sequence encoding a polypeptide having heparanase catalytic activity, wherein said polypeptide shares 70% homology with SEQ ID NO: 10. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection is stated in the previous office action. In response to this rejection applicants have made minor amendments of the claims and traverse the rejection as it applies to the rejected claims. Newly added claim 31 is included in this rejection for the reasons previously stated for the other claims in this rejection.

Applicants submit that applicants specification teaches a number of considerations pertinent to sequence analysis and alignment methodologies of proteins and nucleic acids as well as the use of the amino acid sequence of human heparanase to search for homologous DNA and protein sequences. Applicants further submit that the specification provides methods of protein purification including recombinant

production of proteins as well as an assay for determining heparanase activity.

Applicants submit that based on the above applicants have sufficiently enabled the genus of claimed polynucleotides which encompass any polynucleotide fragment comprising a polynucleotide sequence encoding a polypeptide having heparanase catalytic activity, wherein said polypeptide comprises the amino acid sequence of SEQ ID NO: 10.

Applicants argument is not persuasive because while methods to analyze and identify variants of a known sequence are well known to the skilled artisan, producing variants as claimed by applicants (i.e., encoding a heparanase) requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.

Such guidance has not been provided in the instant specification. As previously stated, the specification does not support the broad scope of the claims which encompass all modifications and fragments of any polynucleotide fragment comprising a polynucleotide sequence encoding a polypeptide having heparanase catalytic activity, wherein said polypeptide shares 70% homology with SEQ ID NO: 10, because the specification does not establish: (A) regions of the encoded protein's structure which

may be modified without effecting heparanase activity; (B) the general tolerance of heparanases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a heparanase protein with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the heparanase activity claimed and the fact that the relationship between the sequence of a polypeptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable, it would require undue experimentation for one skilled in the art to arrive at the majority of those polynucleotides of the claimed genus encoding polypeptides with the claimed heparanase activity.

Applicants note and provide applicants own analysis of the criteria used in the analysis of claims with respect to enablement as summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)): (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

As stated above, without further guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities as encompassed by the claimed genus and this would clearly constitute undue

experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.

Applicants statements regarding the presentation of different heparanases having different degrees of homology as well as a means of the determination of such homology is not considered an adequate "working example" such as to enable the breadth of the claimed genus and while heparanases themselves were known, without the knowledge of their sequence and the relationship between heparanase activity and the amino acid sequence of heparanase, the nature of the invention is not well known and the state of the art does not make up for such a deficiency as was previously stated, while recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

While applicants submission that applicants specification provides the amino acid sequence of human heparanase which is necessary for enabling the identification of candidate amino acids that participate in the heparanase active site, applicants have not

provided such a teaching and taken as a whole, applicants specification is insufficient to enable the scope of such a broad genus.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any polynucleotide fragment comprising a polynucleotide sequence encoding a polypeptide having heparanase catalytic activity, wherein said polypeptide shares 70% homology with SEQ ID NO: 10. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

### ***Terminal Disclaimer***

The terminal disclaimer filed on 8/18/2003 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patent No. 5,968,822 is currently being reviewed and is provisionally accepted. The terminal disclaimer has been recorded.

### ***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).




A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Richard G Hutson, Ph.D.  
Primary Examiner  
Art Unit 1652

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